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L5 and phosphatidylserine	15

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Search History

DATE: Wednesday, January 31, 2007 **Purge Queries** Printable Copy Create Case

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L7	L5 and phosphatidylserine	15	L7
L6	L5 and benzimidazole	2	L6
L5	liposome same arteriosclerosis	99	L5
L4	liposome same arterioosclerosis	0	L4
L3	L1 and benzimidazole	2	L3
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L1	liposome same atherosclerosis	222	L1

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L2: Entry 30 of 30 File: USPT Jul 27, 1993

DOCUMENT-IDENTIFIER: US 5231090 A
TITLE: Treatment for hypercholesterolemia

Brief Summary Text (9):
The affinity of phospholipids for cholesterol provides a basis for the hypothesis that phospholipids, when properly administered, could remove cholesterol from atherosclerotic plaques, and thus reduce the risk for coronary heart disease. Indeed, in experimental animals, intravenous administration of phospholipids has resulted in resolution of atherosclerotic lesions (Friedman et al., Proc. Soc. Exp. Biol. Med. 95:580, 1957; Howard et al., Atherosclerosis 14:17, 1971; Stafford et al., Artery 1(2):105, 1975). Extensive changes in serum lipoproteins in rabbits after intravenous injection of liposomes made of egg yolk phospholipids have been demonstrated. Such changes may have anti-atherogenic effects (Mendez et al., Lipids 23:961, 1988).

Detailed Description Text (3):
Phospholipid-containing compositions suitable for use in the present method comprise at least one phospholipid in a concentration of between, for example, 5% and 50% (w/v). Any natural or synthetic phospholipid, lecithin (phosphatidylcholine), phosphatidylethanolamine and phosphatidylserine, having an affinity for cholesterol can be used in the composition, however, lecithin is preferred.

CLAIMS:

5. The method according to claim 1, wherein said phospholipid is phosphatidylserine.

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L2: Entry 21 of 30 File: USPT Oct 31, 2000

DOCUMENT-IDENTIFIER: US 6139871 A
** See image for Certificate of Correction **
TITLE: Liposome compositions and methods for the treatment of atherosclerosis

Abstract Text (1):
The present invention provides compositions and methods for treating atherosclerosis. The compositions comprise unilamellar liposomes having an average diameter of 100-150 nanometers. Methods for treating atherosclerosis employing the compositions of the present invention are also provided.

Brief Summary Text (2):
The present invention provides pharmaceutical compositions and methods useful for the treatment of atherosclerosis. More particularly, the compositions generally comprise liposomes having an average diameter of about 100-150 nanometers and a pharmaceutically acceptable carrier. The methods generally comprise administering such compositions.

Brief Summary Text (14):
Paradoxically, intravenous infusion of phospholipids and liposomes has been shown to produce regression of atherosclerotic plaques although serum lipid levels are transiently elevated. Williams et al., Perspect. Biol. Med., 27:417-431 (1984). In some instances, however, cholesterol associated with development and progression of atherosclerosis may increase following liposome administration.

Detailed Description Text (2):
The present invention provides pharmaceutical compositions consisting essentially of unilamellar liposomes having an average diameter of about 100-150 nanometers, which liposomes are not bound to a drug; and a pharmaceutically acceptable carrier. Also provided are methods for treating atherosclerosis using the compositions of the present invention.

Detailed Description Text (14):
Other phospholipids suitable for formation of liposomes comprising the compositions of the present invention include, e.g., phosphatidylcholine, phosphatidylglycerol, lecithin, .beta.,.gamma.-dipalmitoyl-.alpha.-lecithin, sphingomyelin, phosphatidylserine, phosphatidic acid, N-(2,3-di(9-(Z)-octadecenyloxy))-prop-1-yl-N,N,N-trimethylammonium chloride, phosphatidylethanolamine, lysolecithin, lysophosphatidylethanolamine, phosphatidylinositol, cephalin, cardiolipin, cerebrosides, dicetylphosphate, dioleoylphosphatidylcholine, dipalmitoylphosphatidylcholine, dipalmitoylphosphatidylglycerol, dioleoylphosphatidylglycerol, palmitoyl-oleoyl-phosphatidylcholine, di-stearoyl-phosphatidylcholine, stearoyl-palmitoyl-phosphatidylcholine, di-palmitoyl-phosphatidylethanolamine, di-stearoyl-phosphatidylethanolamine, di-myrstoyl-phosphatidylserine, di-oleyl-phosphatidylcholine, and the like. Non-phosphorus containing lipids may also be used in the liposomes of the compositions of the present invention. These include, e.g., stearylamine, docecylamine, acetyl palmitate, fatty acid amides, and the like. Additional lipids suitable for use in the liposomes of the present invention are well known to persons of skill in the art and are cited in a variety of well known sources, e.g., McCutcheon's Detergents and Emulsifiers and McCutcheon's Functional Materials, Allured Publishing Co.,

Ridgewood, N.J., both of which are incorporated herein by reference.

Detailed Description Text (17):
The concentration of liposomes in the carrier may vary. Generally, the concentration will be about 20-200 mg/ml, usually about 50-150 mg/ml, and most usually about 100 mg/ml. Persons of skill may vary these concentrations to optimize treatment with different liposomal components or of particular patients. For example, the concentration may be increased to lower the fluid load associated with treatment. This may be particularly desirable in patients having atherosclerosis-associated congestive heart failure or severe hypertension. Alternatively, liposomes composed of irritating lipids may be diluted to low concentrations to lessen inflammation at the site of administration.

Detailed Description Text (20):
Also provided are methods for treating atherosclerosis in an animal. The methods generally comprise administering a liposome composition to the animal, which liposome composition consists essentially of unilamellar liposomes having an average diameter of about 100-150 nanometers. By "treating atherosclerosis", it is meant performing a therapeutic intervention that results in reducing the cholesterol content of at least one atherosclerotic plaque or prophylactically inhibiting or preventing the formation or expansion of an atherosclerotic plaque. Generally, the volume of the atherosclerotic plaque, and hence the degree of obstruction of the vascular lumen, will also be reduced. The present methods are particularly useful for treating atherosclerotic lesions associated with familial hyperlipidemias.

Other Reference Publication (64):
Williams, et al., "Interactions of liposomes with lipoproteins: relevance to drug delivery systems and to the treatment of atherosclerosis," in: Liposomes as drug carriers: recent trends and progress (Gregoriardis G., ed.), pp. 93-111, John Wiley & Sons Ltd: Chichester, England, 1988. Williams, et al., Phospholipid liposomes acquire.

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L7: Entry 13 of 15 File: USPT Jun 20, 2000

DOCUMENT-IDENTIFIER: US 6077529 A
TITLE: Active ingredient system and method of manufacture thereof for transfer of lipophilic and amphiphilic components to target structures

Brief Summary Text (47):
In medicine, the active ingredient system can be used as a medication carrier (drug carrier) to stabilize liposomes relative to blood components. An additional application in medicine is that the active ingredient system is used to produce asymmetrical liposomes for a targeted application of medication (drug targeting). Especially significant is the use of the active ingredient system in handling arteriosclerosis, through which the cholesterol is extracted. For this purpose, cholesterol-free liposomes as the lipid component, are employed in connection with lipid transfer proteins.

CLAIMS:

4. The method of claim 3, wherein the phospholipid is selected from the group consisting of lecithin, phosphatidylserine, phosphatidylglycerol, phosphatidylethanolamine, and phosphatidylinositol.

17. The method of claim 16, wherein the phospholipid is selected from the group consisting of lecithin, phosphatidylserine, phosphatidylglycerol, phosphatidylethanolamine, and phosphatidylinositol.

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L7: Entry 11 of 15 File: USPT Mar 7, 2006

US-PAT-NO: 7008614
DOCUMENT-IDENTIFIER: US 7008614 B2

TITLE: Liposome containing hydrophobic iodine compound and X-ray contrast medium for radiograph comprising the liposome

DATE-ISSUED: March 7, 2006

PRIOR-PUBLICATION:

DOC-ID	DATE
US 20030086875 A1	May 8, 2003

INVENTOR-INFORMATION:

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ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Fuji Photo Film Co., Ltd.	Kanagawa			JP	03

APPL-NO: 10/223461 [PALM]
DATE FILED: August 20, 2002

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	2001-249305	August 20, 2001
JP	2001-249306	August 20, 2001

INT-CL-ISSUED:

TYPE	IPC	DATE	IPC-OLD
IPCP	A61K49/00	20060101	A61K049/00
IPCS	A61K9/127	20060101	A61K009/127

INT-CL-CURRENT:

TYPE	IPC	DATE
CIPP	A61 K 49/00	20060101
CIPS	A61 K 9/127	20060101

US-CL-ISSUED: 424/9.45; 424/450
US-CL-CURRENT: 424/9.45; 424/450

FIELD-OF-CLASSIFICATION-SEARCH: 424/9.4, 424/9.44, 424/9.454, 424/9.455, 424/450,

424/9.45, 424/9.451, 424/9.452, 424/9.453
See application file for complete search history.

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

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	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	5550263	August 1996	Hersl of et al.	554/78
☐	5676928	October 1997	Klaveness et al.	424/9.321

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	CLASS
2 157 283	October 1985	GB	
WO 92/21384	December 1992	WO	
WO 01/82977	November 2001	WO	

OTHER PUBLICATIONS

Radiolabeled Cholesteryl lopanoate\Acetylated Low Density Lipoprotein as a Potential Probe for Visualization of Early Atherosclerotic Lesions in Rabbits Pharmaceutical Research, vol. 16, No. 3 1999 p. 420-426. cited by other
XP-009003943--R .E. Counsell et al., Potential Organ- or Tumor-Imaging Agents. 21. Acyl-Labeled Esters of Cholesterol, J. Med. Chem. (1981), vol. 24, No. 1, pp. 5-6. cited by other
XP-009003944--R. H. Seevers et al.. Potential Organ- or Tumor-Imaging Agents. 22. Acyl-Labeled Cholesterol Esters, J. Med. Chem. (1982), vol. 25, No. 6, pp. 618-621. cited by other
XP-000985456--R. E. Counsell et al., Potential Tumor- or Organ-Imaging Agents XXIV: Chylomicron Remnants as Carriers for Hepatographic Agents, Journal of Pharmaceutical Sciences (1983), vol. 72, No. 8, pp. 898-901. cited by other
XP-002942252--W. Xiao et al., Radiolabeled Cholesteryl Iopanoate/Acetylated Low Density Lipoprotein as a Potential Probe for Visualization of Early Atherosclerotic Lesions in Rabbits, Pharmaceutical Research, NY (1999), vol. 16, No. 3, pp. 420-426. cited by other
XP-002228681--Douglas . A. Bakan et al., Physicochemical Characterization of a Synthetic Lipid Emulsion for Hepatocyte-Selective Delivery of Lipophilic Compounds: Application to Polyiodinated Triglycerides as Contrast Agents for Computed Tomography, Journal of Pharmaceutical Sciences, vol. 85, No. 9 (1996), pp. 908-914. cited by other
Marc A. Longino et al., Formulation of Polyiodinated Triglyceride Analogues in a Chylomicron Remnant-Like Liver-Selective Delivery Vehicle, Pharmaceutical Research, vol. 13, No. 6 (1996), pp. 875-879. cited by oth- er

ART-UNIT: 1618

PRIMARY-EXAMINER: Hartley; Michael

ATTY-AGENT-FIRM: Sughrue Mion, PLLC

ABSTRACT:

A liposome containing a hydrophobic iodine compound represented by the following general formula (I) as a membrane component: R.sup.1--CO.sub.2--R.sup.2 wherein R.sup.1 represents a substituted or unsubstituted 2,3,5-triiodophenyl group or a substituted or unsubstituted 3,4,5-triiodophenyl group; and R.sup.2 represents a hydrocarbon group having 10 or more carbon atoms, and an X-ray contrast medium, which comprises said liposome which is used for radiography of a vascular disease.

11 Claims, 4 Drawing figures

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L1: Entry 6 of 9 File: USPT Mar 6, 2001

DOCUMENT-IDENTIFIER: US 6197333 B1
TITLE: Materials and methods for making improved liposome compositions

Brief Summary Text (3):
Of particular interest to the present invention are the biologically active amphipathic peptides which are members of the family of peptide compounds including vasoactive intestinal peptide (VIP) and growth hormone releasing factor (GRF). More specifically, the invention relates to improved therapeutic methods for delivering peptides in the VIP/GRF family of peptides to targeted tissues through use of improved liposome compositions comprising a member of the VIP/GRF family of peptides and biologically active analogues thereof.

Brief Summary Text (10):
PCT Publication WO 95/27496 and Gao, et al., Life Science 54:247-252 (1994) describe the use of liposomes for delivery of VIP in comparison to its delivery in aqueous solution. Encapsulation of VIP in liposomes was found to protect the peptide from proteolytic degradation and to significantly enhance the ability of VIP and to effect a decrease in mean arterial pressure in comparison to VIP in aqueous solution in hypertensive hamsters. Liposome-associated VIP was found to significantly decrease mean arterial blood pressure for a period of approximately 12 minutes, with lowest blood pressure observed almost 5 minutes after initial administration. The publication also demonstrated binding of VIP in aqueous solution to liposomes and penetration of the peptide into the liposome bilayer. It was speculated that binding of VIP to liposomes might prevent loss of peptide activity either by partitioning of the peptide into the liposome membrane, stabilizing the peptide against proteolysis, or restricting the peptide in a biologically active conformation. Whatever the reason, encapsulation of VIP in liposomes enhanced in vivo biological activity of the peptide by both prolonging the effect and increasing the magnitude of the effect in lowering blood pressure of hypertensive hamsters. Nevertheless, there remains a desire in the art to provide further improvements in the therapeutic and diagnostic delivery of biologically active peptides such as VIP.

Detailed Description Text (5):
The liposomes produced according to the methods of the invention are characterized by improved stability and biological activity and are useful in a variety of therapeutic, diagnostic and/or cosmetic applications. According to one embodiment, the invention comprehends a composition comprising a biologically active liposome product wherein said biologically active amphipathic compound has anti-oxidant activity, anti-aging, anti-wrinkle formation or wound healing capacity. Compositions of this type may be of cosmetic or therapeutic nature. The preferred cosmetic composition includes biologically active VIP. The invention also provides an oral controlled release preparation for the treatment of a gastrointestinal disorder wherein said preparative method further comprises the step of encapsulating the biologically active liposome product in an enteric coating. The oral controlled release preparation is useful in a variety of gastrointestinal disorders including those selected from the group consisting of inflammatory bowel disorder, chronic constipation, Hirschprung's disease, achalasia, infantile hypertrophic pyloric stenosis, and ulcers. The preferred oral preparation includes biologically active VIP. Liposome preparations comprising biologically active VIP

are also a promising therapeutic agent for conditions such as asthma, systemic and pulmonary hypertension, scleroderma, myocardial ischemia, impotence and baldness. The invention further provides methods for preserving a bodily organ, tissue, or cell type for storage and transplantation in a recipient comprising the step of incubating said organ in a liposome composition comprising VIP.

Detailed Description Text (11):
Provisional application 60/014,363 the disclosure of which is hereby incorporated described results described results of use of VIP associated liposomes according to the invention. Specifically, VIP-PEG-liposomes were prepared as follows. DSPE linked to PEG (molecular weight 1,900), PG, PC, and cholesterol (molar ration 0.5:1:5:3.5) were dissolved in chloroform in a round bottom flask. The solution was dried overnight in a rotoevaporator and the resulting film desiccated overnight. The lipid film was rehydrated with saline, pH 6-7, while vortexing, and then sonicated for at least 5 minutes. The liposome preparation thus formed was extruded through stacked Nucleopore filters with pore sizes 200 nm, 100 nm, and 50 nm, respectively, until the mean size of PEG-liposome was 80-100 nm as determined by quasi elastic light scattering. VIP and trehalose, a cryoprotectant, were added to the extruded liposome preparation in polypropylene tubes, the mixture snap-freezed in ethanol- or acetone-dry ice bath for at least 20 minutes, and lyophilized overnight under similar conditions. Free VIP was separated from VIP-PEG-liposomes using Bio Gel A-5m column chromatography. The size of the PEG-liposomes in original solution and VIP-PEG-liposomes was determined by quasi elastic light scattering. Lipid concentration in PEG-liposomes in the original solution and in VIP-PEG-liposomes was determined by inorganic phosphate assay. VIP concentration in VIP-PEG-liposomes was determined by an ELISA assay.

Detailed Description Text (12):
To determine VIP concentration in VIP-PEG-liposomes, 1% sodium dodecyl sulfate, a detergent, was added to an aliquot of the VIP-PEG-liposome preparation to release associated VIP before assay. PEG-liposome and 1% sodium dodecyl sulfate alone did not interfere with the ELISA assay. Non-limiting examples from preliminary experiments using these preparations indicated increased and prolonged biological potency to target tissues of mammals as described below.

Detailed Description Text (24):
Liposomes containing VIP were prepared according to the methods of Gao, et al., Life Sci. 64: PL274-PL252 (1994); Gregoriadis and Florence, Drugs 45:15-28 (1993); MacDonald, et al., Biochem. Biophys. Acta 1061:297-303 (1991); and Suzuki, et al., Life Sci. 57:1451-1457 (1995). Briefly, a lipid composition consisting of egg yolk phosphatidylcholine (Sigma, St. Louis, Mo.), egg yolk phosphatidylglycerol (Sigma), and cholesterol (Sigma) at a 4:1:5 molar ratio (total phospholipid content, 5 mg) was mixed in chloroform (Sigma) and the solvent evaporated to dryness. The dried lipid film was resuspended in 100 .mu.0.15 M NaCl solution containing 0.7 mg VIP by vortex mixing and sonication. The suspension was subjected to five cycles of freeze-thawing using a dry ice-ethanol bath and extruded nine times through two polycarbonate filters (pore size 3 .mu.m; Nuclepore, Pleasanton, Calif.) using a LiposoFast apparatus (capacity of syringe, 0.5 ml; Avestin, Ottawa, ON, Canada). Liposomes were collected using a disposable gel filtration column (Econo-pac lODG, polyacrylamide gel, 10 ml bed vol.) in 0.15 N NaCl [MacDonald, et al., Biochim. Biophys. Acta 1061:297-303(1991)]; the liposome fraction was recovered in the void volume and stored at 4.degree. C. until use.

Detailed Description Text (26):
VIP alone or encapsulated in liposomes was suffused for 7minutes at a concentration of VIP of either 0.05 or 0.1 nmol peptide, and more than 30 minutes elapsed between subsequent applications of the peptide. Changes in arteriolar diameter before, during, and after topical application of VIP were determined as outlined above. The concentrations of VIP used in these experiments were based on previous studies [Gao, et al., Life Sci. 64: PL274-PL252 (1994); Suzuki. et al., Life Sci. 57:1451-

1457 (1995)].

Detailed Description Text (28):
With suffusion of VIP at the same amounts but encapsulated in liposomes, nornotensive animals showed significant, concentration-dependent potentiation and prolongation of vasorelaxant effects in comparison with VIP alone. The maximal response was detected 3 to 4 minutes after suffusion began and significant vasodilation persisted almost 9 minutes after suffusion was stopped. In hamsters with spontaneous hypertension, liposome encapsulated VIP produced a significant vasorelaxant effect of magnitude similar to that observed in the normotensive animals. A maximal effect was detected within 4 minutes from the start of suffusion and significant vasodilation persisted over 3 minutes after suffusion was stopped. Even though encapsulation of VIP in liposomes was able to restore vasorelaxant effects of the peptide in hamsters with spontaneous hypertension to a magnitude similar to that observed in normotensive animals, the duration of effect was significantly shorter.

Detailed Description Text (47):
In a first method of preparation (not contemplated by the invention), VIP was initially mixed with a lipid composition followed by extrusion and repeated freezing and thawing to produce liposomes. Briefly, the dry lipid film was rehydrated with 250 .mu.l 0.15 M saline (0.9% w/w NaCl) containing 0.4 mg VIP (American Peptide Co., Sunnyvale, Calif.). The mixture was vortexed, sonicated for 5 minutes in a 175.5W water bath sonicator (Fisher Scientific, Itasca, Ill.), and freeze-thawed five times in an acetone-dry ice bath. The suspension was extruded through polycarbonate filters using the Liposofast apparatus (pore size 200 nm, AVESTIN, Inc., Ottawa, ON, Canada). The liposome-associated VIP was separated from the free VIP by column chromatography (BioGel A-5m, Bio-Rad Laboratories, Richmond, Calif.) and stored at 4.degree. C. until use. Column elution was carried out using the 15 M saline solution described above. Vesicle size was determined by quasi elastic light scattering [Alkan-Onyuksel, et al., J. Pharm. Sci. In press (1996)] with a Nicomp 270 particle sizer (Particle Sizing Systems, Santa Barbara, Calif.) and liposomes prepared by this method were found to have an average mean diameter of 224.+-.36 nm.

Detailed Description Text (53):
In examining the duration and efficacy of VIP in the two liposome preparations on mean arterial pressure, the following procedure was carried out. Adult mate hamsters with spontaneous hypertension (n=12) were obtained from the Canadian Hybrid Farms (Hall Harbour, Nova Scotia, Canada). Approximately 500 .mu.l each of three test preparations, liposomes prepared by the second method above, VIP in aqueous solution, and liposomes without VIP, were injected administered over the course of 1 minute in the femoral vein. Continuous anesthesia of the animals limited the duration of the experiment to 6 hours.

Detailed Description Text (54):
After injection of 0.1 nmol liposome-associated VIP, a significant and gradual decrease in mean arterial pressure up to 50% was observed in the first 2.5 hours which persisted for the 6 hour observation period of the experiment as shown in FIG. 6. No significant effect on mean arterial pressure was observed using empty liposomes or VIP in aqueous solution. These data suggest that intravenously administered VIP in SSL successfully normalized the mean arterial pressure of hamsters with spontaneous hypertension for at least 6 hours. Interestingly, the dose required to produce normal blood pressure was very low compared to previous observations wherein the same amount of VIP in conventional liposomes produced a 30% decrease in mean arterial pressure of nornotensive hamsters [Gao, et al., Life Sci. 54:PL247PL252 (1994)], but this observation may be attributed to a higher sensitivity of hamsters with spontaneous hypertension to VIP.

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